REMARKS

Claims 180-222 are currently pending in the application and have been examined. Claims 180, 196, 203, and 218 have been amended herein. Support for the amended claims is found, for example, on page 87, lines 18-30. The Examiner is respectfully requested to reconsider her rejections in view of the amendments and remarks as set forth herein below.

I. Claim Rejection-35 USC § 112, first paragraph

Claims 190-195 and 213-217 stand rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse.

Independent claims 190 and 213 are drawn to a virus and a polynucleotide, respectively, comprising a genome that includes a mutation encoding a substitution of amino acid 456 of the L protein by another amino acid. The Examiner contends that because the specification only describes a mutation where the amino acid at position 456 of PIV3 is changed to leucine, and the claims encompass a substitution of any of the 20 amino acids, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides. Applicants strongly disagree.

The Federal Circuit recently stated that a sequence need not appear in a patent specification to support a DNA-based invention provided that the state of the scientific knowledge at the time the application was filed includes such structural information. *Capon et al. v. Eshhar et al. v. Dudas*, 76 USPQ2D 1078 (Fed. Cir. 2005).

In the instant case, a skilled artisan would be fully aware of the structure of the genus of polypeptides claimed. The skilled artisan would merely have to replace the nucleotide sequence encoding an amino acid at the specified location recited in the claims with any of the well-known nucleotide sequences that encode the desired amino acid. Therefore, the present specification adequately supports the independent claims 190 and 213, and their dependents thereon, in compliance with the written description requirement. Applicants respectfully request the instant rejection of claims 190-195 and 213-217 be withdrawn.

II.Claim Rejection-35 USC § 112, second paragraph

Claims 180-222 stand rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the invention. Applicants respectfully traverse.

The Examiner states that the claims are indefinite because the claims recite "attenuated for replication at least 10-fold in the respiratory tract of a primate host infected with said chimeric PIV", without a comparative basis for the term "10-fold."

Independent claims 180, 196, 203 and 218 have been amended to include a comparative basis. The amended claims recite "attenuated for replication at least 10-fold in the respiratory tract of a primate host infected with said chimeric PIV compared to the corresponding wild-type PIV." Because a skilled artisan is able to compare the replicative attenuation level of the inventive viruses to that of the wild-type virus that is modified to produce the chimeric genome or antigenome, the claims are not indefinite.

Independent claims 181, 190, 204 and 213 and their dependents thereon, do not recite any degree of attenuation. Therefore, these claims are seen to be free of the instant rejection.

Independent claim 222 incorporates the language of amended claims 203 and 218, which are now free of this rejection based on the reasons above. Therefore, claims 180-222 are not indefinite. Applicants respectfully request the rejection be reconsidered and withdrawn.

III. Claim Rejections – 35 USC §102

Claims 180-189, 196-212 and 218-220 stand rejected under 35 USC §102(e) as assertedly being anticipated by US Patent No. 5,869,036 to Belshe et al. ("Belshe"). Applicants respectfully traverse.

Belshe discloses nucleic acid constructs encoding from one to three viral proteins (wild-type NP, P and/or L) and cDNA clones of the cp45 genome and hybrids thereof. From the 3' to 5' direction, the cp45 genome is mutated in every gene but the 5' trailer, and, therefore, encodes a mutated L gene. (see FIG. 1 of Belshe relevant to Applicants' arguments regarding cp45). The cp45 virus containing the cp45 genome is unable to be recovered without co-expression of a wild-type L protein at 39.5°C. When the cp45 virus is transfected into cells at 39.5°C, without the wild-type L protein-encoding plasmid, the titer of recovered virus is < 1.0. (See Table 3).

The Examiner should note that every virus described or suggested by Belshe includes a genome encoding a mutated L protein from cp45. Although the Examiner states on page 6 of the office action that "Belshe's construct is a cp45 genome with a wild type L gene introduced" and points to Example 5 to support this contention, it is clear from Example 5 that the cp45 genome does not have the wild-type gene introduced into it. The wild type L gene is in its own plasmid. Furthermore, while viruses produced in the experiment of Example 5 may include a wild-type L protein, the genome packaged by these viruses is a cp45 genome, and so includes the mutated L gene.

In contrast, independent amended claims 180 and 203 are drawn to a chimeric parainfluenza virus, containing a genome or antigenome encoding a wild-type L protein or a polynucleotide encoding such a genome or antigenome, respectively. Because Belshe clearly does not disclose a chimeric genome encoding a wild-type L protein, Belshe cannot anticipate independent claims 180 and 203, and the claims dependent thereon.

As to claims 181 and 204, Belshe discloses hybrid genomes that are derived by substituting the regions encoding the F and HN proteins of cp45 with cDNA copies of corresponding genes of a "target" virus. (See Col 9, lines 54-59 and Col. 10 lines 19-22). The

Examiner should consider that when a substitution occurs, the heterologous segment replaces the segment normally present at the same location; that is, not between two open reading frames, but within or encompassing an ORF. For example, substitution of the HN gene does not result in insertion of the heterologous segment between the HN and L ORFs, but rather in replacement of the entire HN gene, including the gene start sequences, the gene end sequences and the entire HN ORF. Furthermore, Belshe does not disclose the alternative of a hybrid cp45 genome encoding, for example, an additional HN gene inserted between the HN and L open reading frames in a background PIV. Instead Belshe only discloses replacing or substituting one HN gene for another.

In contrast, independent claims 181 and 204 are drawn to a PIV virus or polynucleotide, respectively, containing or encoding a PIV genome with a heterologous open reading frame or antigenic determinant that is inserted between one or more ORFs in adjacent genes. These locations include a) a site between the P and M open reading frames, b) a site between the N and P open reading frames, and c) a site between the HN and L open reading frames. Therefore, independent claims 181 and 204, and claims dependent thereon are not anticipated by Belshe. Applicants respectfully request the rejection be reconsidered and withdrawn.

Additionally, independent amended claims 196 and 218 also have been rejected as anticipated by Belshe. However, a claim can only be anticipated if each and every element as set forth in the claim is found either expressly or inherently in a single reference. Amended independent claims 196 and 218 both recite the element of a heterologous gene segment operatively linked to a gene start sequence and a gene end sequence of a PIV genome or antigenome. Operatively linking a gene segment encoding a heterologous open reading frame to gene start and gene end sequences of a PIV viral genome is not disclosed, expressly or inherently, anywhere in the Belshe reference. Because all of the elements of amended independent claims 196 and 218 and claims dependent thereon are not present in the reference, reconsideration and withdrawal of this rejection are respectfully requested.

Claims 180-189, 196-212 and 218-220 are not anticipated by Belshe for the reasons stated above. Applicants respectfully request the rejection of these claims under 35 USC § 102(e) over Belshe be reconsidered and withdrawn.

Rejections under § 103

The Examiner has rejected claims 196-201 and claims 218-222 under 35 USC § 103(a) as allegedly obvious over Belshe. Applicants respectfully traverse.

In order to establish *prima facie* obviousness, the combined references must teach or suggest all of the elements of a claim. Amended independent claims 196 and 218 and claims dependent thereon, are drawn to isolated viruses comprising a PIV genome (or antigenome) and polynucleotides, respectively, wherein the genomes or polynucleotides encode a heterologous antigenic determinant that is located between a gene start and a gene end sequence. Although Belshe fails to teach or suggest the insertion of heterologous open reading frames encoding antigenic determinants between gene start and gene end sequences, the Examiner alleges that insertion of an open reading frame "would only be *appropriate* between a gene start and a gene end sequence." (Emphasis added.) However, Belshe only discloses that the "gene sequence which encodes [the desired protein] …may be substituted for the corresponding sequence in the cp45 genome." (See Col. 8 lines 59-61.) Additionally, Belshe's FIG. 1 does not depict any non-translated, intergenic sequences. Therefore, a person of skill in the art, without the benefit of the instant application, would understand that Belshe teaches substituting, for example, all of the HN gene sequence, including transcription regulating sequences, of the target virus for the corresponding sequence in a cp45 background genome. Belshe does not suggest, as the Examiner asserts, that "one would be motivated to use the gene start and gene end sequences in order to retain as much stability as possible when expressing the heterologous genes." This benefit is recognized only when viewed in conjunction with the instant specification. According to the MPEP at 2142, "impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art." Therefore, independent claims 196 and 218 and their respective dependent claims are not obvious over Belshe.

For the above reasons, claims 196-201 and claims 218-222 are non-obvious over Belshe. Applicants request that the instant rejection be reconsidered and withdrawn.

Rejection under non-statutory double-patenting

The Examiner presents a number of provisional obviousness-type double patenting rejections. Applicants request that these issues should be held in abeyance since prosecution is continuing in both cases and the issue may be resolved by amendments in the various applications. See MPEP 804. If necessary, Applicants will file a Terminal Disclaimer following the procedure outlined in the above-mentioned section of the MPEP.

The present application well-describes and claims patentable subject matter. The favorable action of allowance of the pending claims and passage of the application to issue is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell (Reg. No. 36,623) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

By _____

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